**Review Article** | Breast Imaging

eISSN 2005-8330
https://doi.org/10.3348/kjr.2020.0093
Korean J Radiol 2021;22(1):9-22

Korean Journal of Radiology
KJR

# Diffusion-Weighted Magnetic Resonance Imaging of the Breast: Standardization of Image Acquisition and Interpretation

Su Hyun Lee, MD, PhD[1], Hee Jung Shin, MD, PhD[2], Woo Kyung Moon, MD, PhD[1]

[1]Department of Radiology, Seoul National University Hospital, Seoul, Korea; [2]Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Diffusion-weighted (DW) magnetic resonance imaging (MRI) is a rapid, unenhanced imaging technique that measures the motion of water molecules within tissues and provides information regarding the cell density and tissue microstructure. DW MRI has demonstrated the potential to improve the specificity of breast MRI, facilitate the evaluation of tumor response to neoadjuvant chemotherapy and can be employed in unenhanced MRI screening. However, standardization of the acquisition and interpretation of DW MRI is challenging. Recently, the European Society of Breast Radiology issued a consensus statement, which described the acquisition parameters and interpretation of DW MRI. The current article describes the basic principles, standardized acquisition protocols and interpretation guidelines, and the clinical applications of DW MRI in breast imaging.
**Keywords:** *Diffusion-weighted MRI; Dense breast; Standardization; Supplemental screening; Cancer*

## INTRODUCTION

Dynamic contrast-enhanced (DCE) magnetic resonance imaging (MRI) is the standard protocol for the breast MRI, which evaluates the morphologic and kinetic features of breast lesions. It is the most sensitive and accurate imaging modality used for the detection and characterization of breast cancer. DCE MRI can detect breast cancers that were occult on mammography and ultrasound at an earlier stage and consequently reduce the occurrence of interval cancers (1-8). However, high cost, long duration of examination and the use of contrast agents have limited the widespread use of DCE MRI in breast cancer screening. Although abbreviated breast MRI has solved some of the aforementioned problems, it still requires the use of contrast agents, which limits its use in population-based screening (9). Recently, there have been growing public concerns over the unknown health effects of gadolinium deposition in brain and other tissues, as a consequence of repeated gadolinium contrast agent injections (10, 11). Therefore, in the current clinical scenario, research involving the development of an unenhanced, rapid and less expensive screening tool that complements mammography and is potentially safer than DCE MRI has become increasingly important.

Diffusion-weighted (DW) imaging is a functional MRI technique that can produce contrast in tissues without using gadolinium contrast medium injections and the process of whole breast imaging can be completed within a few minutes (12). Various useful clinical applications of DW MRI in breast imaging have been explored so far and a growing number of imaging centers are incorporating DW MRI into the routine clinical breast MRI examination. However, DW MRI acquisition parameters are not standardized and there is no uniform method of interpretation; consequently, resulting in a large variability in image quality and diagnostic performance, which has

**Received:** February 5, 2020 **Revised:** May 6, 2020
**Accepted:** May 9, 2020
This study was supported by a grant from the National R&D Program for Cancer Control, Ministry of Health and Welfare, Republic of Korea (HA17C0056).
**Corresponding author:** Woo Kyung Moon, MD, PhD, Department of Radiology, Seoul National University Hospital, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea.
• E-mail: moonwk@snu.ac.kr

prevented the incorporation of DW MRI findings into the Breast Imaging Reporting and Data System (BI-RADS). Standardized acquisition protocols and interpretation guidelines are required, in order to facilitate the clinical application of DW MRI and to enable cross-institutional comparisons. Recently, the European Society of Breast Radiology (EUSOBI) issued a consensus statement, which describes the acquisition parameters for standard breast DW MRI sequences (13).

In the present article, the authors briefly review the basic principles, optimized image acquisition and standardized interpretation guidelines for DW MRI and subsequently explain the clinical applications of DW MRI in breast imaging. The extensions of DW MRI to characterize diffusion directionality and perfusion fractions within tissues, namely the diffusion tensor imaging (14, 15) and intravoxel incoherent motion imaging (16), are the fields of active research that have the potential to provide valuable information. However, the aforementioned imaging modalities are not routinely used in clinical breast imaging and hence, they are not included in the current review.

## Basics Physics of DW MRI

DW MRI involves the use of a specific sequence in which the diffusion or random motion of water molecules in a tissue primarily contributes to image contrast. The sequence, originally proposed by Stejskal and Tanner (17), was based on a spin echo sequence that has symmetric diffusion sensitizing gradients, inserted before and after the 180° refocusing pulse. Paired pulsed gradients cause the signal loss from diffusing water spins, but stationary water spins remain unaffected. The reduction in the intensity of DW MRI signal is proportional to the water mobility and is commonly described by the monoexponential equation:

$S_D = S_0 e^{-b*ADC}$, where $S_D$ is the signal intensity with diffusion-weighting, $S_0$ is the signal intensity without diffusion-weighting, b is the diffusion sensitization factor and ADC is the apparent diffusion coefficient. The b value is a factor that reflects the degree of diffusion-weighting, which is determined by the amplitude and duration of the sensitizing gradients and the time interval between the gradient pair (expressed in sec/mm$^2$). ADC is defined as the average area occupied by a water molecule per unit time (expressed in mm$^2$/sec) and can be calculated using the image acquisitions at two or more different b values.

The standard DW MRI sequence produces two sets of images (Fig. 1): T2-weighted reference images obtained without diffusion gradients ($S_0$), and DW images obtained with diffusion gradients ($S_D$) that reflect the water mobility. The parametric ADC map is created to enable the diffusion quantification without T2 shine-through effects. An area of restricted diffusion, such as a breast cancer lesion, appears bright on the DW image and dark on the ADC map (Fig. 1) (18).

## Image Acquisition

### Standardized Acquisition Parameters

The acquisition parameters can affect the quality of DW MRI and ADC values. Although different parameters may need to be used for DW MRI, depending on the MRI machine, several acquisition parameters are suggested to ensure the quality of breast DW MRI. Recently, the EUSOBI working group issued a consensus statement, which outlined the minimum set of acquisition parameters that should be

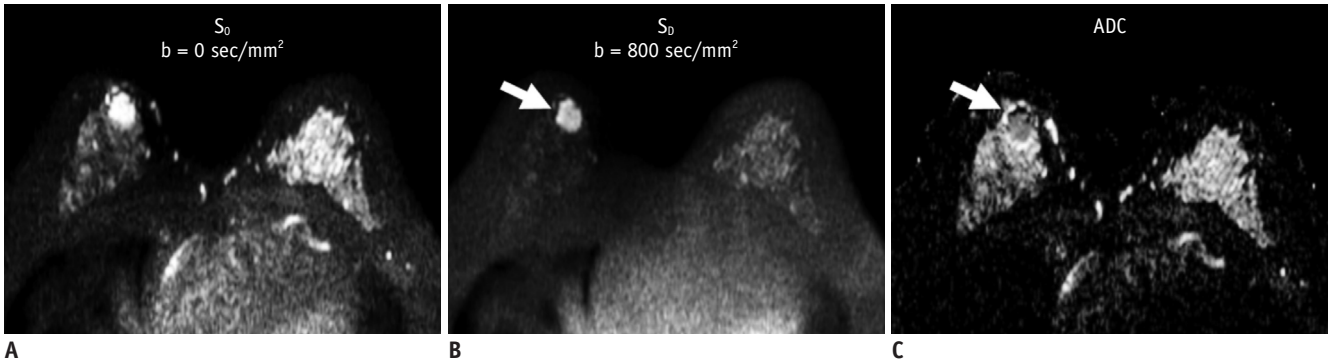


**Fig. 1. Standard DW image sets.**
DW image sets consist of T2-weighted reference image obtained without diffusion gradients **(A)**, DW images obtained with diffusion gradients (b value of 800 sec/mm$^2$) **(B)**, and the parametric ADC map **(C)**. An area of restricted diffusion with breast cancer (arrow) appears bright on the DW image and dark on the ADC map. ADC = apparent diffusion coefficient, DW = diffusion-weighted, $S_0$ = signal intensity with b = 0 s/mm$^2$, $S_D$ = signal intensity with b = 800 s/mm$^2$


https://doi.org/10.3348/kjr.2020.0093

Korean Journal of Radiology
KJR

met in clinical practice and proposed a guideline for the standardized acquisition protocol (Table 1) (13). According to the aforementioned guidelines, breast DW MRI should be performed in a closed bore magnet at field strength of 1.5T or higher with a maximum gradient strength of at least 30 mT/m, using a dedicated breast coil with at least four channels, and before the administration of the contrast agent when possible (19). In combination with the spin echo, single-shot or multishot echo-planar imaging (EPI) should be used as the readout sequence in axial planes of bilateral breasts with a minimum in-plane resolution of 2 x 2 $mm^2$ and a section thickness of 4 mm or less. The echo time should be minimized to the lowest possible value, in order to reduce susceptibility artifacts, and the repetition time should be 3000 msec or more. In practice, all EPI sequences are fat-suppressed to prevent ghosting and the potential underestimation of ADC values. Among the different methods employed for the fat suppression, spectral adiabatic inversion recovery is preferred over the short tau inversion recovery. Parallel imaging with an acceleration factor of 2 is recommended, in order to reduce the distortion attributable to susceptibility artifacts. An ADC map, calculated using at least two b values, needs to be generated.

### Choice of b Value

The choice of b value is important because it determines the ADC value and affects the signal-to-noise ratio of the image and the contrast-to-noise ratio of the lesion (20-23). The ADC values decrease with the increase in b values, owing to the non-Gaussian nature of water diffusion in tissues (13). Hence, using a common b value is important for the purpose of standardization and comparison. Recently, a high b value of 800 sec/$mm^2$ and a low b value of 0–50 sec/$mm^2$ were chosen by the EUSOBI working group as a good compromise for the standardization and accurate estimation of breast ADCs (13). However, in terms of qualitative lesion detection, DW MRI with a very high b value of 1200–1500 sec/$mm^2$ may be optimal because higher b values increase the visibility of the lesion and the specificity of lesion detection, despite the lower signal-to-noise ratios and longer duration of imaging (Fig. 2) (20, 22). Hence, when DW MRI is used for screening examinations, where both the lesion detection and accurate ADC quantitation are priorities, acquisition with three different ranges of b values, i.e., 0–50 sec/$mm^2$, 800

**Table 1. Standardized Breast DW MRI Acquisition Parameters**

| Parameter | Minimum Requirement* | Requirement for Screening Examination† |
|---|---|---|
| Equipment | | |
| Magnet field strength | ≥ 1.5T | 3T |
| Type of coil | Dedicated breast coil with ≥ 4 channels | 16 or 18 channels |
| Timing of acquisition | Before contrast injection, when possible | Before contrast injection |
| Acquisition parameter | | |
| Type of sequence | EPI based | EPI based (single-shot or multishot) |
| Orientation | Axial | Axial |
| Field of view | Both breasts with or without covering the axillary region | Both breasts with covering the axillary region |
| In-plane resolution | ≤ 2 x 2 $mm^2$ | ≤ 1.3 x 1.3 $mm^2$ |
| Slice thickness | ≤ 4 mm | ≤ 3 mm |
| Number of b values | 2 | 3 |
| Lowest b value | 0 sec/$mm^2$ (not exceeding 50 sec/$mm^2$) | 0 sec/$mm^2$ |
| High b value | 800 sec/$mm^2$ | 800 sec/$mm^2$ and additional acquisition of 1200 sec/$mm^2$ |
| Fat saturation | SPAIR | SPAIR |
| TE | Minimum possible | Minimum possible |
| TR | ≥ 3000 ms | ≥ 7500 ms |
| Acceleration | Parallel imaging (factor ≥ 2) | Parallel imaging (factor ≥ 2) |
| Post-processing | Generation of ADC maps | Generation of ADC maps, additional generation of MIP |

*Recommendation of the European Society of Breast Radiology (13), †Recommended in Korean multicenter screening DW MRI study. ADC = apparent diffusion coefficient, DW = diffusion-weighted, EPI = echo-planar imaging, MIP = maximum intensity projection, MRI = magnetic resonance imaging, SPAIR = spectral adiabatic inversion recovery, STIR = short tau inversion recovery, TE = echo time, TR = repetition time


https://doi.org/10.3348/kjr.2020.0093

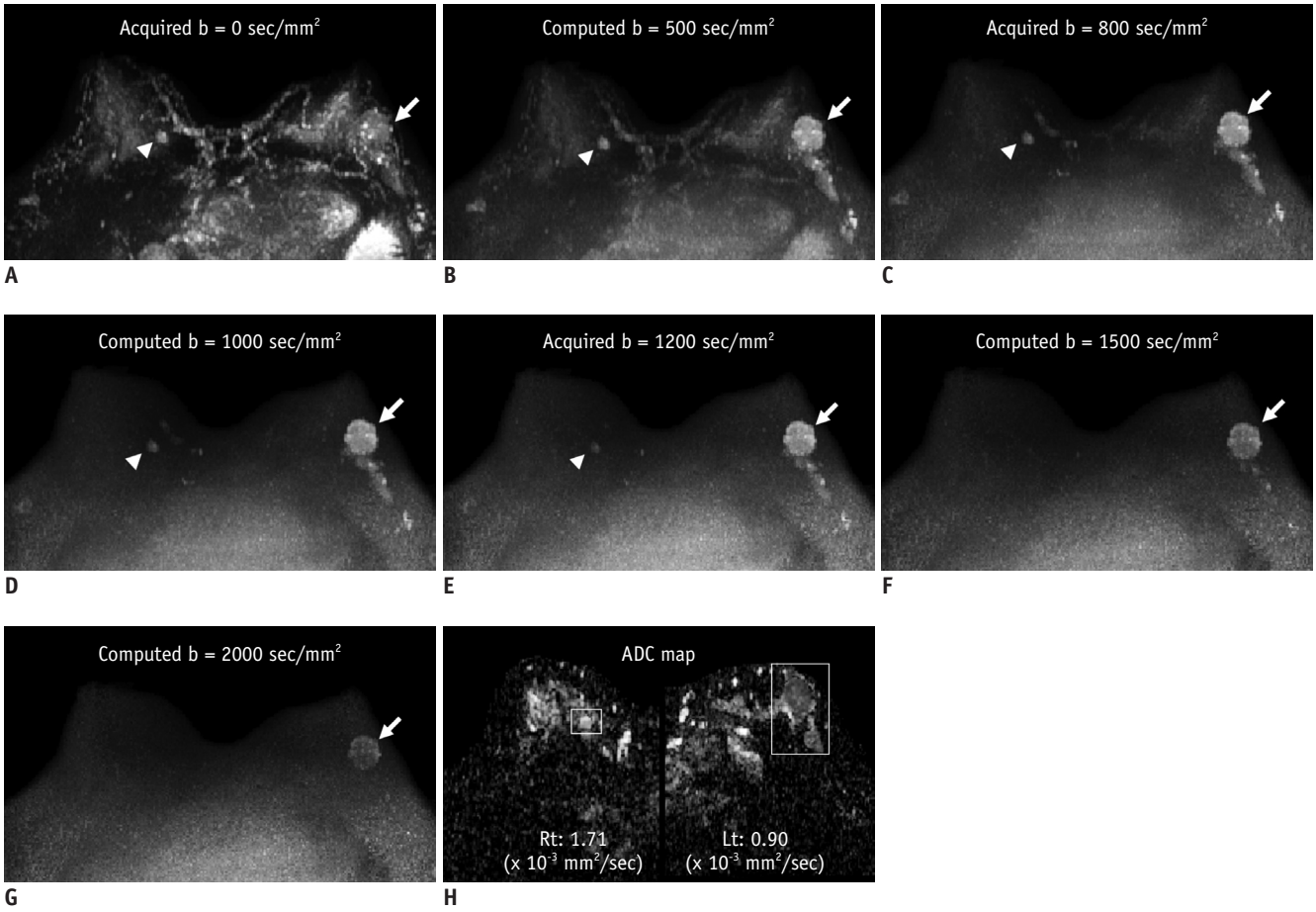


**Fig. 2. Effect of b value on the signal intensity of normal breast parenchyma and benign and malignant breast lesions.**
As the b value increases **(A-G)**, the signal intensity of normal breast parenchyma (background diffusion signal) and a biopsy-proven fibroadenoma (arrowhead) decreases, whereas the signal intensity of an invasive ductal carcinoma (arrow) remains high, increasing the lesion visibility and specificity for lesion detection, despite the lower signal-to-noise ratio. On the ADC map calculated using the b values of 0 sec/mm$^2$ and 800 sec/mm$^2$ **(H)**, the breast cancer appears as dark signal intensity (ADC value, 0.90 x $10^{-3}$ mm$^2$/sec), while the fibroadenoma appears as high signal intensity (ADC value, 1.71 x $10^{-3}$ mm$^2$/sec).

sec/mm$^2$, and 1200–1500 sec/mm$^2$, may be recommended (Table 1) (19). The diffusion-sensitizing gradients are usually applied in three orthogonal directions (x, y, or z axes) and the acquired images are automatically averaged into a final combined image.

## Advanced Acquisition Technique

Conventional DW MRI is performed using a single-shot EPI, in which all k-space lines, which form the image, are acquired during a single excitation. Thus, EPI is a rapid MRI technique, capable of acquiring individual MR slices within a time frame of 50–100 msec, consequently minimizing the effects of patient movement (24). However, EPI suffers from susceptibility artifacts or distortions, low signal-to-noise ratio and spatial blurring, particularly at higher field strengths. Furthermore, in case of small lesions (< 1 cm in size), the typical DW MRI axial in-plane spatial resolution of 2 x 2 mm$^2$ and section thickness of 4 mm can result in a significant partial volume effect. In order to facilitate the use of DW MRI as an unenhanced screening method, its ability to detect and characterize breast lesions, including subcentimeter lesions, should be enhanced.

Currently, advanced DW MRI techniques to improve the image quality and achieve higher spatial resolution are under research. Such techniques include the readout-segmented EPI, a multishot EPI approach in which k-space sampling occurs with a small number (three to six) of excitations (shots) and each shot divides the k-space into so called segments. Multishot EPI reduces the required matrix size acquired per shot, thus, reducing the susceptibility artifacts and allowing for higher spatial resolution and total image matrix size at the expense of the acquisition time (Fig. 3) (25-28). Currently, this sequence is marketed by a vendor (Siemens Healthineers) under the trade name


https://doi.org/10.3348/kjr.2020.0093

Korean Journal of Radiology
KJR

RESOLVE (readout segmentation of long variable echo trains). Another advanced technique that aims to improve the spatial resolution of DW MRI is the reduced field-of-view (rFOV). The rFOV technique permits high resolution DW MRI of the targeted volume by decreasing the required number of k-space lines while reducing the distortion. The technique is commercially available from several vendors as FOCUS (GE Medical Systems), ZOOMit (Siemens Healthineers) and iZOOM (Philips Healthcare). Several studies have reported that DW MRI with rFOV improved the lesion conspicuity, compared to DW MRI with full FOV (Fig. 3) (29-31). However, the absolute ADCs in DW MRI with rFOV were lower, compared to DW MRI with full FOV ($p < 0.001$), which may render the previously published ADC cutoff values less useful in the interpretation of DW MRI with rFOV (30, 31).

## Postprocessing

Postprocessing may also improve the image quality of DW MRI by correcting the geometric distortions arising from field inhomogeneities and other factors (32). However, a previous study reported that up to 10% of the breast DW MRI scans showed spatial mismatch between the DW images that could not be corrected by a registration algorithm, consequently emphasizing the importance of implementing techniques in minimizing the effects of eddy-currents and patient movement at the time of acquisition (33). Other postprocessing techniques, including maximum intensity projections (MIPs), which select the matrix voxel with the highest signal intensity from the multiple sections to produce a single image of the whole examination volume, or the fusion of high b value DW MRI to unenhanced T1-weighted or T2-weighted images, improve the lesion detection and conspicuity on DW MRI by enhancing the image display (26, 27, 34-36). Last of all, the computed DW MRI is a technique used for obtaining high b value images from those acquired at lower b values. The aforementioned

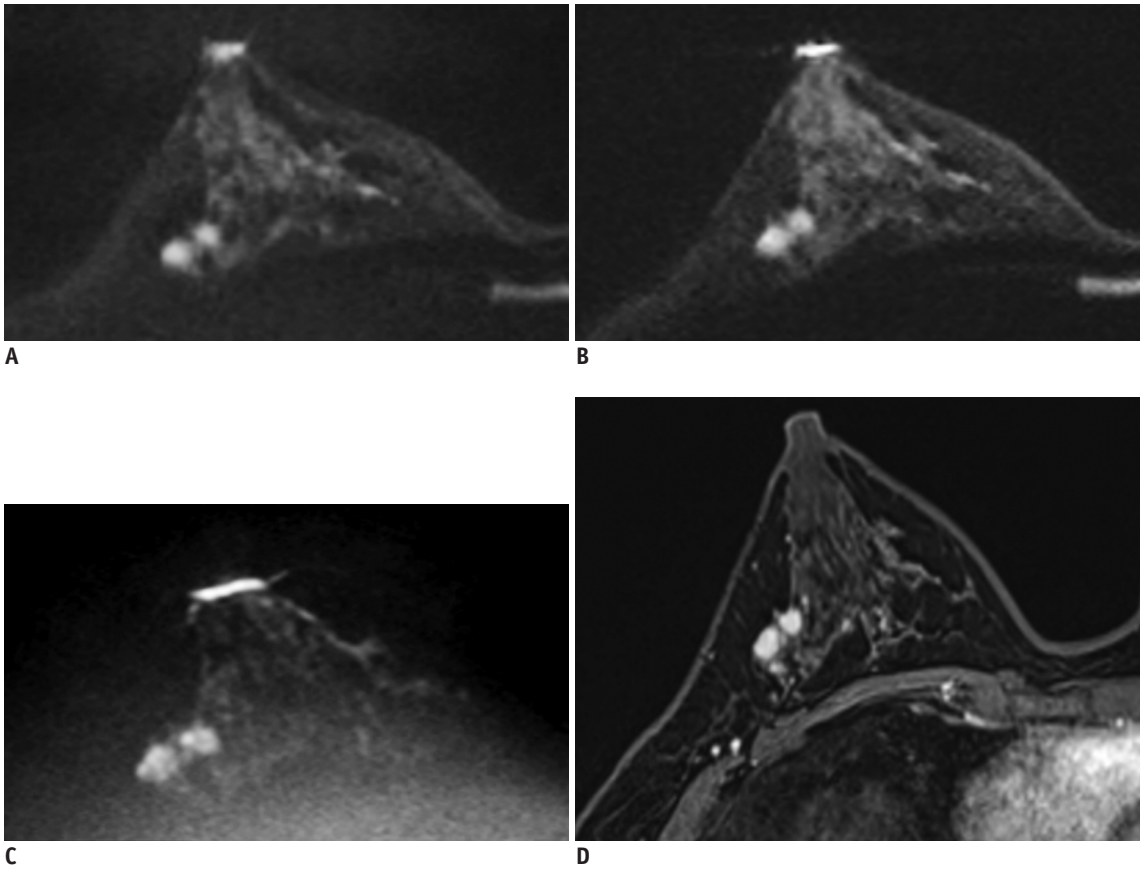


**Fig. 3. DW MRI acquired using different acquisition techniques at the b value of 1000 sec/mm$^2$.**
**A.** Single-shot EPI with in-plane resolution of 1.3 x 1.3 mm$^2$. **B.** Readout-segmented EPI with in-plane resolution of 1.3 x 1.3 mm$^2$. **C.** Reduced field of view technique with in-plane resolution of 0.59 x 0.59 mm$^2$. The T1-weighed dynamic contrast-enhanced MRI with in-plane resolution of 0.9 x 0.9 mm$^2$. **D.** Demonstrates two adjacent irregular enhancing masses. Core needle biopsy and conservation surgery revealed two adjacent grade 2 invasive ductal carcinomas of size 2.4 cm and 0.5 cm. EPI = echo-planar imaging, MRI = magnetic resonance imaging


https://doi.org/10.3348/kjr.2020.0093

technique can provide high b value images with good image quality and high background suppression, while maintaining a short duration of imaging, and provide the flexibility for retrospective generation of images at any b value for optimal interpretation (37, 38).

## Image Interpretation

### Imaging Features of Normal Breast Parenchyma and Background Diffusion Signals

In order to develop standardized interpretation criteria, it is necessary to understand the appearance and normative range of ADCs in the breast parenchyma on DW MRI. The normal breast parenchymal tissue exhibits a high signal intensity on DW MRI with low b value, as the low b value image is primarily T2-weighted. As the b value increases, the signal intensity of normal breast tissue gets suppressed (Fig. 2). The degree of background diffusion signal on high b value DW MRI can vary among women and can be visually assessed according to the 4-point scale of minimum, mild, moderate and marked (Fig. 4); similar to the background parenchymal enhancement in DCE MRI (39). Several previous studies have attempted to establish a normative range of breast parenchymal ADC and the reported mean ADCs of normal breast tissue varies over a wide range from 1.51 x $10^{-3}$ to 2.09 x $10^{-3}$ $mm^2$/sec (with the maximum b

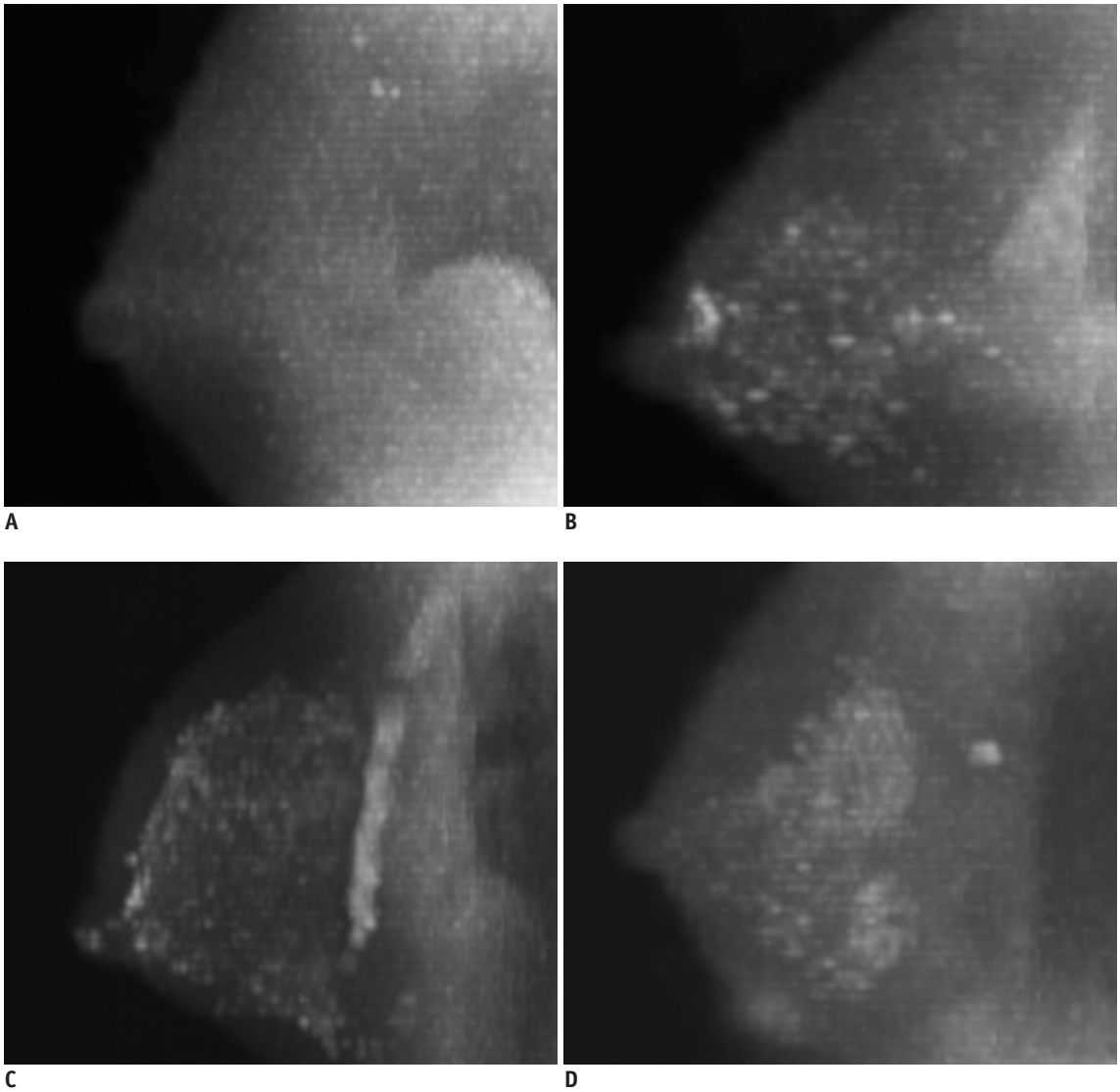


**Fig. 4. The degree of background diffusion signals on DW MRI.**
MIP images of DW MRI acquired at the b value of 1200 sec/$mm^2$ displaying minimal **(A)**, mild **(B)**, moderate **(C)**, and marked **(D)** background diffusion signals. MIP = maximum intensity projection


https://doi.org/10.3348/kjr.2020.0093

Korean Journal of Radiology
KJR

values ranging from 600 to 1000 sec/mm$^2$) (12). Although hormonal fluctuations may influence the breast ADC values, a recent study reported that the ADC values of normal breast parenchyma are not significantly affected by the menstrual cycle (40). Conversely, breast density can affect the ADC values of the breast parenchyma and the ADC values tend to be lower in fatty breasts than in dense breasts, which is most probably attributable to the intravoxel partial volume averaging with fat (41).

### Lesion Detection and Qualitative Assessment on DW MRI

In a multiparametric breast MRI protocol, lesion detection can primarily be based on the evaluation of contrast-enhanced sequences (13). When DW MRI is employed as a stand-alone screening tool, lesions, defined as unique areas of high signal intensity that are distinct from background signals, must be detected on high b value DW MRI (19).

The use of MIP of DW MRI enables a quick overview of the entire breast volume and shortens the reading time for lesion detection (Fig. 5); similar to the use of MIPs for abbreviated contrast-enhanced MRI protocols (35). If lesions with high signal intensity are detected in the DW MRI, the location, size and morphology of the lesions can be assessed qualitatively. Morphology of the lesions on DW images can be categorized as foci, masses, or non-mass lesions (Fig. 6). In case of the lesions categorized as masses, shape (round/oval, irregular) and internal signal pattern (homogeneous, heterogeneous, rim) can be reported, whereas in non-mass lesions, distribution (focal, regional, linear, segmental) and internal signal pattern

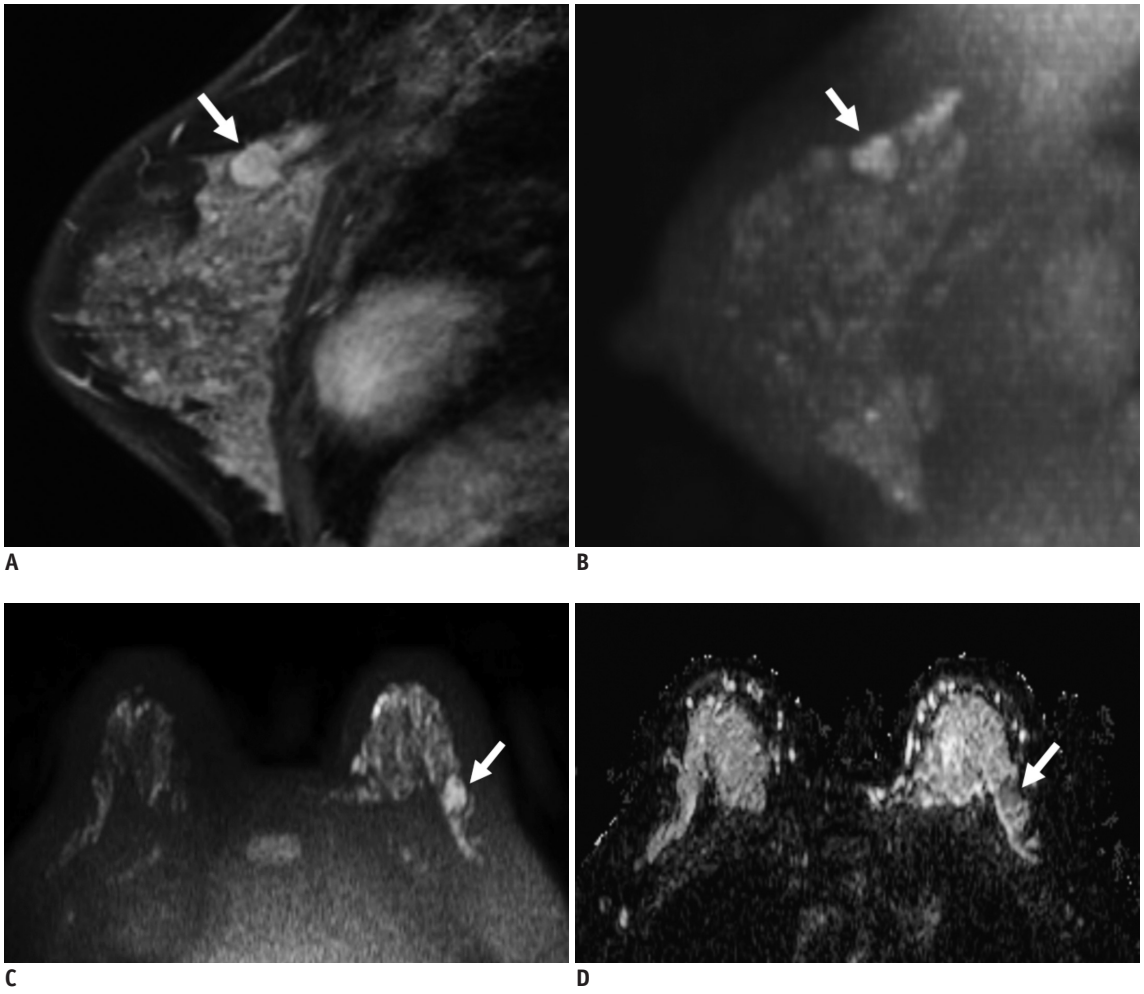


**Fig. 5. Lesion detection and characterization on DW MRI.**
Sagittal image from dynamic contrast-enhanced MRI **(A)** shows an irregular enhancing mass (arrow) in the left breast at the 1 o'clock position. On reconstructed sagittal MIP of DW MRI obtained with a b value of 1200 sec/mm$^2$ **(B)**, a mass of high signal intensity (arrow) distinct from the background diffusion signal is easily detectable. On the corresponding axial images of DW MRI obtained with a b value of 800 sec/mm$^2$ **(C)** and ADC map **(D)**, an irregular mass of high signal intensity (arrow) with a low mean ADC of 0.97 x $10^{-3}$ mm$^2$/sec is demonstrated. Core needle biopsy and conservation surgery revealed a grade 2 invasive ductal carcinoma of size 1.5 cm.


https://doi.org/10.3348/kjr.2020.0093

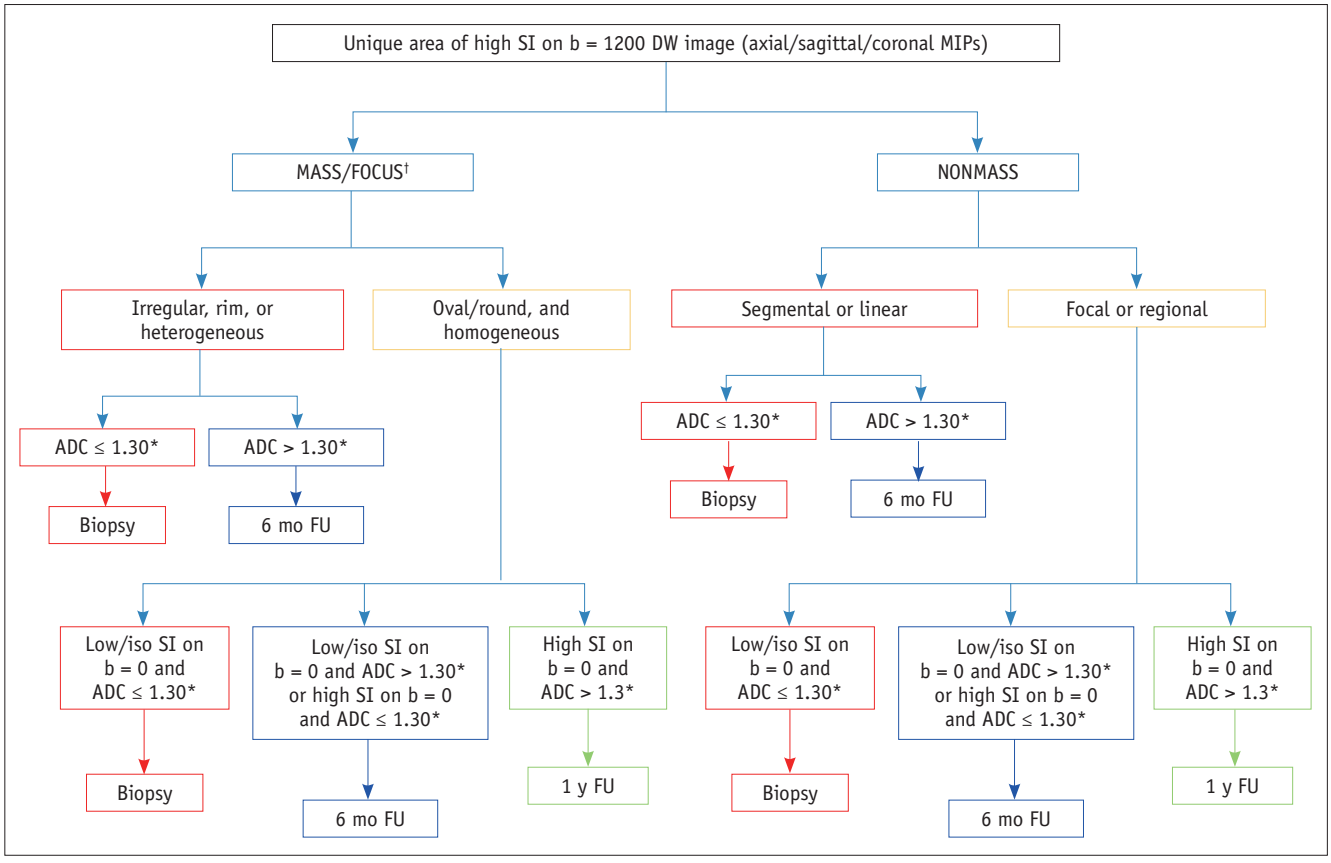


**Fig. 6. Interpretation guideline used in a prospective multicenter study (clinicaltrials.gov Identifier: NCT03835897) for 3T screening DW MRI with b values of 0, 800, and 1200 sec/mm$^2$.** *ADC map is calculated from b = 0 and 800 sec/mm$^2$ DW image, †Focus is evaluated based on both SI on b = 0 sec/mm$^2$ and ADC value (x $10^{-3}$ mm$^2$/sec). FU = follow-up, SI = signal intensity

(homogeneous, heterogeneous) can be reported (13). Qualitative evaluation of the lesion morphology might be of assistance in avoiding the misclassification of false-positive benign lesions, such as complicated cysts or fibroadenomas, as well as to avoid misdiagnosis of false-negative malignant lesions, including mucinous carcinoma or invasive breast cancer with extensive necrosis (42).

### Quantitative Assessment on DW MRI

Lesions detected on high b value DW MRI require cross-correlation with the ADC map, in order to rule out "T2 shine-through" effects and the lesions with true restricted diffusion should exhibit low ADCs. Quantitative ADC values (expressed in the units of $10^{-3}$ mm$^2$/sec) are measured by drawing a region of interest (ROI) on the lesion on the ADC map. The ROI should be drawn completely within the lesion, consistent with the hyperintense areas on high b value DW MRI, while avoiding normal tissue and areas of necrosis, hemorrhage, or fat by cross referencing with the contrast-enhanced T1-weighted images or unenhanced T1- and T2-weighted images, if available (12, 43). On the subject of the size of the ROI to be used, two multicenter trials in the United States employed the method of drawing the ROI for the entire lesion and measuring the average ADC across a lesion (44, 45). However, according to a recently published international expert agreement, the use of a small ROI placed on the darkest part of the lesion on the ADC map that represents the most suspicious area is suggested as the preferred method for measuring ADC values, in order to reduce the inter- and intra-reader variability and improve the diagnostic performance of breast DW MRI (13). In any case, the type of ROI (whole lesion or focused) used for ADC measurement should be reported.

In view of the fact that the ADC values are dependent on the b factor, a specific ADC threshold value, which can be used to differentiate between benign and malignant lesions, has not been established. The EUSOBI proposed the use of ADC values measured at the high b value of 800 sec/mm$^2$ for the purpose of standardization and they proposed the classification of diffusion level in lesions as


https://doi.org/10.3348/kjr.2020.0093

Korean Journal of Radiology
KJR

follows: very low (range of ADC, ≤ 0.9 x $10^{-3}$ $mm^2$/sec); low (range of ADC, 0.9–1.3 x $10^{-3}$ $mm^2$/sec); intermediate (range of ADC, 1.3–1.7 x $10^{-3}$ $mm^2$/sec); high (range of ADC, 1.7–2.1 x $10^{-3}$ $mm^2$/sec) and very high (range of ADC, > 2.1 x $10^{-3}$ $mm^2$/sec) (13). The authors also noted that when the ADC value is unrealistically high (> 3 x $10^{-3}$ $mm^2$/sec) or low (< 0.5 x $10^{-3}$ $mm^2$/sec), repositioning the ROI may be required to eliminate the bias from adjacent noise regions, such as voxels containing fat (13). The previously reported ADC cutoff values to distinguish between benign and malignant lesions ranged from 1.1 x $10^{-3}$ to 1.6 x $10^{-3}$ $mm^2$/sec (46). The choice of ADC cutoff values to differentiate between benign and malignant lesions can depend on the expectations from DW MRI (12). Higher cutoff values should be selected to increase the sensitivity and lower cutoff values are desirable to improve the specificity. A recent multicenter study, the American College of Radiology Imaging Network 6702 trial, evaluated the ADC values of undiagnosed breast lesions (BI-RADS 3, 4, or 5) identified through DCE MRI and proposed 1.68 x $10^{-3}$ $mm^2$/sec as the cutoff value that can improve the specificity without affecting the sensitivity (45). An ongoing multicenter prospective clinical trial (clinicaltrials.gov Identifier: NCT03835897) in South Korea, which employs the DW MRI for primary breast cancer screening in high-risk women, uses an interpretation algorithm that combines quantitative b value measurements with qualitative morphology evaluation and uses an ADC cutoff value of 1.3 x $10^{-3}$ $mm^2$/sec (Fig. 6).

### False-Negative and False-Positive Findings

The DW MRI signals and ADC values of various breast lesions are summarized in Table 2. DW MRI cannot detect all the malignancies, which can be identified through DCE MRI. False-negative findings on DW MRI can be caused by two primary factors: the characteristics of the carcinoma itself, such as low cellularity or non-mass morphologic type, and the limited resolution of the DW MRI technique, in addition to other technical issues including artifacts, inadequate fat suppression, or low signal-to-noise ratio. Mucinous carcinoma is a well-known cause of false-negative results, owing to the low cellularity and high mucin content (47). Moreover, triple-negative cancer with extensive necrosis can present with high ADC values (48). Ductal carcinoma *in situ* (DCIS) and invasive lobular carcinoma are typically non-mass type carcinomas and are more likely to be missed by DW MRI, compared to the invasive ductal carcinoma, owing to the low conspicuity (49). Finally, considering the typical in-plane spatial resolution (2 x 2 $mm^2$) and section thickness (3–5 mm) of DW MRI, small cancers (1 cm or less in size) are expected to be less detectable or incorrectly characterized on account of the partial volume effects (50, 51). Technical advances in breast DW MRI may improve the detection and characterization of smaller cancer foci and non-mass lesions.

Examples of false-positive findings on breast DW MRI include mastitis, abscesses and hematomas, complicated cysts, intramammary lymph nodes, intraductal papilloma, atypical ductal hyperplasia and fibroadenomas with high cellularity (33, 46, 47, 52, 53). According to previous reports, the diffusion of water molecules is not only restricted in the environments with high cellularity, but also in the regions of intracellular and extracellular edema, regions of high viscosity in abscesses and hematomas, coagulated blood or proteinaceous debris within ducts and cysts, and areas with a high degree of fibrosis (18, 54, 55). Furthermore, artifactual signal at the nipple, an area prone to susceptibility-based distortion on DW MRI, can result in false-positive findings (49, 50).

**Table 2. Signal Intensity on DW MRI and ADC Value for Various Breast Lesions**

| Lesion Type | Pathologic Condition | Signal Intensity on DW MRI with High b value* | Signal Intensity on DW MRI with Low b value | ADC Value |
|---|---|---|---|---|
| High cellularity, high viscosity fluid | Cancer, intraductal papilloma, mastitis/abscess, hemorrhage | High | Intermediate | Decreased |
| Medium cellularity, high water content, proteinaceous fluid | Fibroadenoma with increased cellularity, complicated cyst | High to intermediate | Intermediate to high | Intermediate to high |
| Low cellularity, high water content | Cyst, fibroadenoma, mucinous cancer | Intermediate to low | High | Increased |
| Low cellularity, low water content | Fibrous tissue, calcification | Low | Low | Decreased |

Signal intensity may differ depending on the imaging parameters. Higher b values result in overall lower signal from all tissues. *b = 800–1500 sec/$mm^2$.


https://doi.org/10.3348/kjr.2020.0093

## Clinical Applications of DW MRI: Current Evidence and Possibilities

### Lesion Characterization and Diagnosis

The primary and most explored application of DW MRI in breast imaging has been to use DW MRI as a supplement to DCE MRI in the differential diagnosis of benign and malignant lesions. Two meta-analyses, which evaluated the diagnostic performance of quantitative breast DW MRI, demonstrated that the overall specificity of DW MRI is superior, compared to DCE MRI (56, 57). Several studies, including one prospective multicenter trial, have consistently reported that supplementing DCE MRI with DW MRI improves the specificity (75–84%), compared to the specificity of DCE MRI alone (67–72%); thus, potentially obviating unnecessary biopsies (33, 45, 58, 59).

In addition to the differentiation between benign and malignant lesions, DW MRI has the potential to characterize malignancies in terms of tumor grade and hormone receptor status, and distinguish between invasive and noninvasive diseases. It has been reported that high-grade invasive cancers have lower ADC values, compared to intermediate- or low-grade cancers and DCIS (60-62). ADC values were shown to be higher in estrogen receptor (ER)-negative tumors, compared to the ER-positive tumors; whereas the human epidermal growth factor receptor-enriched tumors exhibited the highest ADC values (48, 63-65). Considering the whole scenario, further studies involving larger cohorts from multiple institutions are required, in order to determine the association between ADC and tumor biomarkers.

### Monitoring and Prediction of Treatment Response

Neoadjuvant chemotherapy is increasingly being used for breast cancer treatment. Cytotoxic effects of chemotherapy, including cell lysis, apoptosis and necrosis, cause alterations in the cell membrane integrity, which increases the water mobility in the extracellular space that occurs before the advent of morphologic changes. Multiple studies have reported that the increase in tumor ADC, in response to treatment, is detectable earlier than the changes in size or vascularity, as measured by DCE MRI, which may denote an early indication of the treatment efficacy (66-68). Moreover, some studies have found that the pretreatment tumor ADC values are predictive of the pathological response; baseline ADC values were observed to be lower in clinical responders, compared to non-responders (69-72). Residual disease after neoadjuvant chemotherapy may be predicted with greater accuracy by means of the changes in ADC, compared to the changes on DCE MRI in some cases (44). However, in the current literature, there is a wide variability in opinions regarding the utility of DW MRI to monitor and predict treatment response; probably due to the differences in study design, including patient characteristics, treatment regimens, chemotherapy cycle and image timing, DW MRI acquisition parameters and methods of ADC measurement. In this scenario, further investigation is required, in order to validate ADC as a predictive biomarker for treatment response.

### Axillary Lymph Nodes

DW MRI is a promising tool, which can be used to differentiate between metastatic and nonmetastatic axillary lymph nodes in patients with breast cancer. According to a meta-analysis, which included ten published studies, the mean ADC value of metastatic lymph nodes was significantly lower, compared to that of nonmetastatic lymph nodes and the pooled sensitivity and specificity of DW MRI were 89% and 83%, respectively (73). Another systematic review reported that DW MRI showed higher median sensitivity (84.2%) and negative predictive value (90.6%), compared to DCE MRI (60% and 80%); however, the sensitivity and negative predictive value was observed to be inferior to unenhanced T1-weighted/T2-weighted MRI (88.4% and 94.7%) (74). Scaranelo et al. (75) reported that axillary lymph node evaluation with DW MRI is reproducible and reliable, but the additional benefit over conventional T1-weighted/T2-weighted MRI is minimal. The use of dedicated axillary protocols may improve the diagnostic performance in nodal staging (76).

### Unenhanced MRI for Breast Cancer Screening

DW MRI has the potential to be employed as a stand-alone tool for unenhanced MRI for breast cancer screening. In a study involving 118 mammographically occult lesions (91 benign, 27 malignant), DW MRI could detect 89% of the DCE MRI-detected malignancies, when the readers were not blinded to the images from DCE MRI (56). In another nonblinded study involving 60 mammographically occult cancers, DW MRI detected more cancers, compared to the MRI-guided focused ultrasound (78% and 63%, respectively, $p = 0.049$) (77). In previous blinded reader studies in which the readers assessed only unenhanced MRI sequences, including DW MRI with or without nonenhanced T1/T2-weighted image, the sensitivity of DW MRI in various study designs ranged from 45% to 94% (27, 34, 49, 50, 78, 79).


https://doi.org/10.3348/kjr.2020.0093

Korean Journal of Radiology
KJR

The limitations of DW MRI for breast cancer screening include the lack of evidence from larger prospective studies and the difficulty of targeting the lesions in vacuum assisted MRI-guided biopsy of the lesions detected only through DW MRI, particularly in the case of small lesions (less than 1 cm in size) (80). Currently, ongoing prospective clinical trials are investigating the role of DW MRI in screening high-risk women (NCT03835897) or women with dense breasts (NCT03607552), using standardized and optimized DW MRI protocols. Further evidence from the prospective multicenter clinical studies and technical advances in DW MRI will facilitate the use of DW MRI in unenhanced breast cancer screening.

## CONCLUSION

In summary, DW MRI is a rapid, unenhanced technique, which shows the potential to be employed in breast cancer screening and can be used in the accurate differential diagnosis of the breast lesions found in DCE MRI and the monitoring of breast cancer response to neoadjuvant chemotherapy. Standardized acquisition and interpretation protocols can improve the image quality of DW MRI and reduce the variability in results. High resolution DW MRI using advanced acquisition techniques and postprocessing will facilitate better detection and characterization of subcentimeter cancers and reduce the false-negative and false-positive findings. The results from ongoing prospective clinical studies using standardized and optimized protocols will facilitate the use of DW MRI in unenhanced breast cancer screening.

### Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

### ORCID iDs

Su Hyun Lee
https://orcid.org/0000-0002-0171-8060
Hee Jung Shin
https://orcid.org/0000-0002-3398-1074
Woo Kyung Moon
https://orcid.org/0000-0001-8931-3772

## REFERENCES

1. Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med* 2004;351:427-437
2. Warner E, Plewes DB, Hill KA, Causer PA, Zubovits JT, Jong RA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA* 2004;292:1317-1325
3. Kuhl CK, Schrading S, Leutner CC, Morakkabati-Spitz N, Wardelmann E, Fimmers R, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. *J Clin Oncol* 2005;23:8469-8476
4. Leach MO, Boggis CR, Dixon AK, Easton DF, Eeles RA, Evans DG, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). *Lancet* 2005;365:1769-1778
5. Lehman CD, Blume JD, Thickman D, Bluemke DA, Pisano E, Kuhl C, et al. Added cancer yield of MRI in screening the contralateral breast of women recently diagnosed with breast cancer: results from the International Breast Magnetic Resonance Consortium (IBMC) trial. *J Surg Oncol* 2005;92:9-15; discussion 15-16
6. Warner E, Hill K, Causer P, Plewes D, Jong R, Yaffe M, et al. Prospective study of breast cancer incidence in women with a BRCA1 or BRCA2 mutation under surveillance with and without magnetic resonance imaging. *J Clin Oncol* 2011;29:1664-1669
7. Berg WA, Zhang Z, Lehrer D, Jong RA, Pisano ED, Barr RG, et al. Detection of breast cancer with addition of annual screening ultrasound or a single screening MRI to mammography in women with elevated breast cancer risk. *JAMA* 2012;307:1394-1404
8. Passaperuma K, Warner E, Causer PA, Hill KA, Messner S, Wong JW, et al. Long-term results of screening with magnetic resonance imaging in women with BRCA mutations. *Br J Cancer* 2012;107:24-30
9. Kuhl CK, Schrading S, Strobel K, Schild HH, Hilgers RD, Bieling HB. Abbreviated breast magnetic resonance imaging (MRI): first postcontrast subtracted images and maximum-intensity projection-a novel approach to breast cancer screening with MRI. *J Clin Oncol* 2014;32:2304-2310
10. Kanda T, Fukusato T, Matsuda M, Toyoda K, Oba H, Kotoku J, et al. Gadolinium-based contrast agent accumulates in the brain even in subjects without severe renal dysfunction: evaluation of autopsy brain specimens with inductively coupled plasma mass spectroscopy. *Radiology* 2015;276:228-232
11. McDonald RJ, McDonald JS, Kallmes DF, Jentoft ME, Murray DL, Thielen KR, et al. Intracranial gadolinium deposition after contrast-enhanced MR imaging. *Radiology* 2015;275:772-782
12. Partridge SC, McDonald ES. Diffusion weighted magnetic resonance imaging of the breast: protocol optimization, interpretation, and clinical applications. *Magn Reson Imaging*

 https://doi.org/10.3348/kjr.2020.0093 

*Clin N Am* 2013;21:601-624
13. Baltzer P, Mann RM, Iima M, Sigmund EE, Clauser P, Gilbert FJ, et al. Diffusion-weighted imaging of the breast—a consensus and mission statement from the EUSOBI International Breast Diffusion-Weighted Imaging working group. *Eur Radiol* 2020;30:1436-1450
14. Kim JY, Kim JJ, Kim S, Choo KS, Kim A, Kang T, et al. Diffusion tensor magnetic resonance imaging of breast cancer: associations between diffusion metrics and histological prognostic factors. *Eur Radiol* 2018;28:3185-3193
15. Luo J, Hippe DS, Rahbar H, Parsian S, Rendi MH, Partridge SC. Diffusion tensor imaging for characterizing tumor microstructure and improving diagnostic performance on breast MRI: a prospective observational study. *Breast Cancer Res* 2019;21:102
16. Song SE, Cho KR, Seo BK, Woo OH, Park KH, Son YH, et al. Intravoxel incoherent motion diffusion-weighted MRI of invasive breast cancer: correlation with prognostic factors and kinetic features acquired with computer-aided diagnosis. *J Magn Reson Imaging* 2019;49:118-130
17. Stejskal EO, Tanner JE. Spin diffusion measurements: spin echoes in the presence of a time-dependent field gradient. *J Chem Phys* 1965;42:288-292
18. Guo Y, Cai YQ, Cai ZL, Gao YG, An NY, Ma L, et al. Differentiation of clinically benign and malignant breast lesions using diffusion-weighted imaging. *J Magn Reson Imaging* 2002;16:172-178
19. Amornsiripanitch N, Bickelhaupt S, Shin HJ, Dang M, Rahbar H, Pinker K, et al. Diffusion-weighted MRI for unenhanced breast cancer screening. *Radiology* 2019;293:504-520
20. Tamura T, Murakami S, Naito K, Yamada T, Fujimoto T, Kikkawa T. Investigation of the optimal b-value to detect breast tumors with diffusion weighted imaging by 1.5-T MRI. *Cancer Imaging* 2014;14:11
21. Iima M, Yano K, Kataoka M, Umehana M, Murata K, Kanao S, et al. Quantitative non-Gaussian diffusion and intravoxel incoherent motion magnetic resonance imaging: differentiation of malignant and benign breast lesions. *Invest Radiol* 2015;50:205-211
22. Han X, Li J, Wang X. Comparison and optimization of 3.0 T breast images quality of diffusion-weighted imaging with multiple b-values. *Acad Radiol* 2017;24:418-425
23. Peters NH, Vincken KL, van den Bosch MA, Luijten PR, Mali WP, Bartels LW. Quantitative diffusion weighted imaging for differentiation of benign and malignant breast lesions: the influence of the choice of b-values. *J Magn Reson Imaging* 2010;31:1100-1105
24. Poustchi-Amin M, Mirowitz SA, Brown JJ, McKinstry RC, Li T. Principles and applications of echo-planar imaging: a review for the general radiologist. *Radiographics* 2001;21:767-779
25. Porter DA, Heidemann RM. High resolution diffusion-weighted imaging using readout-segmented echo-planar imaging, parallel imaging and a two-dimensional navigator-based reacquisition. *Magn Reson Med* 2009;62:468-475
26. Shin HJ, Chae EY, Choi WJ, Ha SM, Park JY, Shin KC, et al. Diagnostic performance of fused diffusion-weighted imaging using unenhanced or postcontrast T1-weighted MR imaging in patients with breast cancer. *Medicine (Baltimore)* 2016;95:e3502
27. Kang JW, Shin HJ, Shin KC, Chae EY, Choi WJ, Cha JH, et al. Unenhanced magnetic resonance screening using fused diffusion-weighted imaging and maximum-intensity projection in patients with a personal history of breast cancer: role of fused DWI for postoperative screening. *Breast Cancer Res Treat* 2017;165:119-128
28. Baltzer PAT, Bickel H, Spick C, Wengert G, Woitek R, Kapetas P, et al. Potential of noncontrast magnetic resonance imaging with diffusion-weighted imaging in characterization of breast lesions: intraindividual comparison with dynamic contrast-enhanced magnetic resonance imaging. *Invest Radiol* 2018;53:229-235
29. Singer L, Wilmes LJ, Saritas EU, Shankaranarayanan A, Proctor E, Wisner DJ, et al. High-resolution diffusion-weighted magnetic resonance imaging in patients with locally advanced breast cancer. *Acad Radiol* 2012;19:526-534
30. Barentsz MW, Taviani V, Chang JM, Ikeda DM, Miyake KK, Banerjee S, et al. Assessment of tumor morphology on diffusion-weighted (DWI) breast MRI: diagnostic value of reduced field of view DWI. *J Magn Reson Imaging* 2015;42:1656-1665
31. Park JY, Shin HJ, Shin KC, Sung YS, Choi WJ, Chae EY, et al. Comparison of readout segmented echo planar imaging (EPI) and EPI with reduced field-of-view diffusion-weighted imaging at 3t in patients with breast cancer. *J Magn Reson Imaging* 2015;42:1679-1688
32. Partridge SC, Nissan N, Rahbar H, Kitsch AE, Sigmund EE. Diffusion-weighted breast MRI: clinical applications and emerging techniques. *J Magn Reson Imaging* 2017;45:337-355
33. Partridge SC, DeMartini WB, Kurland BF, Eby PR, White SW, Lehman CD. Quantitative diffusion-weighted imaging as an adjunct to conventional breast MRI for improved positive predictive value. *AJR Am J Roentgenol* 2009;193:1716-1722
34. Telegrafo M, Rella L, Stabile Ianora AA, Angelelli G, Moschetta M. Unenhanced breast MRI (STIR, T2-weighted TSE, DWIBS): an accurate and alternative strategy for detecting and differentiating breast lesions. *Magn Reson Imaging* 2015;33:951-955
35. Bickelhaupt S, Laun FB, Tesdorff J, Lederer W, Daniel H, Stieber A, et al. Fast and noninvasive characterization of suspicious lesions detected at breast cancer X-ray screening: capability of diffusion-weighted MR imaging with MIPs. *Radiology* 2016;278:689-697
36. Bickelhaupt S, Tesdorff J, Laun FB, Kuder TA, Lederer W, Teiner S, et al. Independent value of image fusion in unenhanced breast MRI using diffusion-weighted and morphological T2-weighted images for lesion characterization in patients with recently detected BI-RADS 4/5 x-ray mammography findings. *Eur Radiol* 2017;27:562-569


https://doi.org/10.3348/kjr.2020.0093

37. Blackledge MD, Leach MO, Collins DJ, Koh DM. Computed diffusion-weighted MR imaging may improve tumor detection. *Radiology* 2011;261:573-581
38. O'Flynn EA, Blackledge M, Collins D, Downey K, Doran S, Patel H, et al. Evaluating the diagnostic sensitivity of computed diffusion-weighted MR imaging in the detection of breast cancer. *J Magn Reson Imaging* 2016;44:130-137
39. Hahn SY, Ko ES, Han BK, Lim Y, Gu S, Ko EY. Analysis of factors influencing the degree of detectability on diffusion-weighted MRI and diffusion background signals in patients with invasive breast cancer. *Medicine (Baltimore)* 2016;95:e4086
40. Kim JY, Suh HB, Kang HJ, Shin JK, Choo KS, Nam KJ, et al. Apparent diffusion coefficient of breast cancer and normal fibroglandular tissue in diffusion-weighted imaging: the effects of menstrual cycle and menopausal status. *Breast Cancer Res Treat* 2016;157:31-40
41. Partridge SC, Singer L, Sun R, Wilmes LJ, Klifa CS, Lehman CD, et al. Diffusion-weighted MRI: influence of intravoxel fat signal and breast density on breast tumor conspicuity and apparent diffusion coefficient measurements. *Magn Reson Imaging* 2011;29:1215-1221
42. Radovic N, Ivanac G, Divjak E, Biondic I, Bulum A, Brkljacic B. Evaluation of breast cancer morphology using diffusion-weighted and dynamic contrast-enhanced MRI: intermethod and interobserver agreement. *J Magn Reson Imaging* 2019;49:1381-1390
43. Bickel H, Pinker K, Polanec S, Magometschnigg H, Wengert G, Spick C, et al. Diffusion-weighted imaging of breast lesions: region-of-interest placement and different ADC parameters influence apparent diffusion coefficient values. *Eur Radiol* 2017;27:1883-1892
44. Partridge SC, Zhang Z, Newitt DC, Gibbs JE, Chenevert TL, Rosen MA, et al. Diffusion-weighted MRI findings predict pathologic response in neoadjuvant treatment of breast cancer: the ACRIN 6698 multicenter trial. *Radiology* 2018;289:618-627
45. Rahbar H, Zhang Z, Chenevert TL, Romanoff J, Kitsch AE, Hanna LG, et al. Utility of diffusion-weighted imaging to decrease unnecessary biopsies prompted by breast MRI: a trial of the ECOG-ACRIN cancer research group (A6702). *Clin Cancer Res* 2019;25:1756-1765
46. Tsushima Y, Takahashi-Taketomi A, Endo K. Magnetic resonance (MR) differential diagnosis of breast tumors using apparent diffusion coefficient (ADC) on 1.5-T. *J Magn Reson Imaging* 2009;30:249-255
47. Woodhams R, Matsunaga K, Kan S, Hata H, Ozaki M, Iwabuchi K, et al. ADC mapping of benign and malignant breast tumors. *Magn Reson Med Sci* 2005;4:35-42
48. Youk JH, Son EJ, Chung J, Kim JA, Kim EK. Triple-negative invasive breast cancer on dynamic contrast-enhanced and diffusion-weighted MR imaging: comparison with other breast cancer subtypes. *Eur Radiol* 2012;22:1724-1734
49. McDonald ES, Hammersley JA, Chou SH, Rahbar H, Scheel JR, Lee CI, et al. Performance of DWI as a rapid unenhanced technique for detecting mammographically occult breast cancer in elevated-risk women with dense breasts. *AJR Am J Roentgenol* 2016;207:205-216
50. Kazama T, Kuroki Y, Kikuchi M, Sato Y, Nagashima T, Miyazawa Y, et al. Diffusion-weighted MRI as an adjunct to mammography in women under 50 years of age: an initial study. *J Magn Reson Imaging* 2012;36:139-144
51. Pinker K, Moy L, Sutton EJ, Mann RM, Weber M, Thakur SB, et al. Diffusion-weighted imaging with apparent diffusion coefficient mapping for breast cancer detection as a stand-alone parameter: comparison with dynamic contrast-enhanced and multiparametric magnetic resonance imaging. *Invest Radiol* 2018;53:587-595
52. Brandão AC, Lehman CD, Partridge SC. Breast magnetic resonance imaging: diffusion-weighted imaging. *Magn Reson Imaging Clin N Am* 2013;21:321-336
53. Parsian S, Rahbar H, Allison KH, Demartini WB, Olson ML, Lehman CD, et al. Nonmalignant breast lesions: ADCs of benign and high-risk subtypes assessed as false-positive at dynamic enhanced MR imaging. *Radiology* 2012;265:696-706
54. Koh DM, Collins DJ. Diffusion-weighted MRI in the body: applications and challenges in oncology. *AJR Am J Roentgenol* 2007;188:1622-1635
55. Woodhams R, Kakita S, Hata H, Iwabuchi K, Umeoka S, Mountford CE, et al. Diffusion-weighted imaging of mucinous carcinoma of the breast: evaluation of apparent diffusion coefficient and signal intensity in correlation with histologic findings. *AJR Am J Roentgenol* 2009;193:260-266
56. Partridge SC, Demartini WB, Kurland BF, Eby PR, White SW, Lehman CD. Differential diagnosis of mammographically and clinically occult breast lesions on diffusion-weighted MRI. *J Magn Reson Imaging* 2010;31:562-570
57. Zhang L, Tang M, Min Z, Lu J, Lei X, Zhang X. Accuracy of combined dynamic contrast-enhanced magnetic resonance imaging and diffusion-weighted imaging for breast cancer detection: a meta-analysis. *Acta Radiol* 2016;57:651-660
58. Ei Khouli RH, Jacobs MA, Mezban SD, Huang P, Kamel IR, Macura KJ, et al. Diffusion-weighted imaging improves the diagnostic accuracy of conventional 3.0-T breast MR imaging. *Radiology* 2010;256:64-73
59. Spick C, Pinker-Domenig K, Rudas M, Helbich TH, Baltzer PA. MRI-only lesions: application of diffusion-weighted imaging obviates unnecessary MR-guided breast biopsies. *Eur Radiol* 2014;24:1204-1210
60. Razek AA, Gaballa G, Denewer A, Nada N. Invasive ductal carcinoma: correlation of apparent diffusion coefficient value with pathological prognostic factors. *NMR Biomed* 2010;23:619-623
61. Costantini M, Belli P, Rinaldi P, Bufi E, Giardina G, Franceschini G, et al. Diffusion-weighted imaging in breast cancer: relationship between apparent diffusion coefficient and tumour aggressiveness. *Clin Radiol* 2010;65:1005-1012
62. Bickel H, Pinker-Domenig K, Bogner W, Spick C, Bagó-Horváth


 https://doi.org/10.3348/kjr.2020.0093 

Z, Weber M, et al. Quantitative apparent diffusion coefficient as a noninvasive imaging biomarker for the differentiation of invasive breast cancer and ductal carcinoma in situ. *Invest Radiol* 2015;50:95-100
63. Martincich L, Deantoni V, Bertotto I, Redana S, Kubatzki F, Sarotto I, et al. Correlations between diffusion-weighted imaging and breast cancer biomarkers. *Eur Radiol* 2012;22:1519-1528
64. Jeh SK, Kim SH, Kim HS, Kang BJ, Jeong SH, Yim HW, et al. Correlation of the apparent diffusion coefficient value and dynamic magnetic resonance imaging findings with prognostic factors in invasive ductal carcinoma. *J Magn Reson Imaging* 2011;33:102-109
65. Choi SY, Chang YW, Park HJ, Kim HJ, Hong SS, Seo DY. Correlation of the apparent diffusion coefficiency values on diffusion-weighted imaging with prognostic factors for breast cancer. *Br J Radiol* 2012;85:e474-e479
66. Pickles MD, Gibbs P, Lowry M, Turnbull LW. Diffusion changes precede size reduction in neoadjuvant treatment of breast cancer. *Magn Reson Imaging* 2006;24:843-847
67. Sharma U, Danishad KK, Seenu V, Jagannathan NR. Longitudinal study of the assessment by MRI and diffusion-weighted imaging of tumor response in patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy. *NMR Biomed* 2009;22:104-113
68. Galbán CJ, Ma B, Malyarenko D, Pickles MD, Heist K, Henry NL, et al. Multi-site clinical evaluation of DW-MRI as a treatment response metric for breast cancer patients undergoing neoadjuvant chemotherapy. *PLoS One* 2015;10:e0122151
69. Iacconi C, Giannelli M, Marini C, Cilotti A, Moretti M, Viacava P, et al. The role of mean diffusivity (MD) as a predictive index of the response to chemotherapy in locally advanced breast cancer: a preliminary study. *Eur Radiol* 2010;20:303-308
70. Park SH, Moon WK, Cho N, Song IC, Chang JM, Park IA, et al. Diffusion-weighted MR imaging: pretreatment prediction of response to neoadjuvant chemotherapy in patients with breast cancer. *Radiology* 2010;257:56-63
71. Li XR, Cheng LQ, Liu M, Zhang YJ, Wang JD, Zhang AL, et al. DW-MRI ADC values can predict treatment response in patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy. *Med Oncol* 2012;29:425-431
72. Richard R, Thomassin I, Chapellier M, Scemama A, de Cremoux P, Varna M, et al. Diffusion-weighted MRI in pretreatment prediction of response to neoadjuvant chemotherapy in patients with breast cancer. *Eur Radiol* 2013;23:2420-2431
73. Sui WF, Chen X, Peng ZK, Ye J, Wu JT. The Diagnosis of metastatic axillary lymph nodes of breast cancer by diffusion weighted imaging: a meta-analysis and systematic review. *World J Surg Oncol* 2016;14:155
74. Kuijs VJ, Moossdorff M, Schipper RJ, Beets-Tan RG, Heuts EM, Keymeulen KB, et al. The role of MRI in axillary lymph node imaging in breast cancer patients: a systematic review. *Insights Imaging* 2015;6:203-215
75. Scaranelo AM, Eiada R, Jacks LM, Kulkarni SR, Crystal P. Accuracy of unenhanced MR imaging in the detection of axillary lymph node metastasis: study of reproducibility and reliability. *Radiology* 2012;262:425-434
76. Schipper RJ, Paiman ML, Beets-Tan RG, Nelemans PJ, de Vries B, Heuts EM, et al. Diagnostic performance of dedicated axillary T2- and diffusion-weighted MR imaging for nodal staging in breast cancer. *Radiology* 2015;275:345-355
77. Amornsiripanitch N, Rahbar H, Kitsch AE, Lam DL, Weitzel B, Partridge SC. Visibility of mammographically occult breast cancer on diffusion-weighted MRI versus ultrasound. *Clin Imaging* 2018;49:37-43
78. Yabuuchi H, Matsuo Y, Sunami S, Kamitani T, Kawanami S, Setoguchi T, et al. Detection of non-palpable breast cancer in asymptomatic women by using unenhanced diffusion-weighted and T2-weighted MR imaging: comparison with mammography and dynamic contrast-enhanced MR imaging. *Eur Radiol* 2011;21:11-17
79. Trimboli RM, Verardi N, Cartia F, Carbonaro LA, Sardanelli F. Breast cancer detection using double reading of unenhanced MRI including T1-weighted, T2-weighted STIR, and diffusion-weighted imaging: a proof of concept study. *AJR Am J Roentgenol* 2014;203:674-681
80. Berger N, Varga Z, Frauenfelder T, Boss A. MRI-guided breast vacuum biopsy: localization of the lesion without contrast-agent application using diffusion-weighted imaging. *Magn Reson Imaging* 2017;38:1-5


https://doi.org/10.3348/kjr.2020.0093